

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 62589-PCT (71699)		Date of mailing (day/month/year) 24 AUG 2005
FOR FURTHER ACTION See paragraph 2 below		
International application No. PCT/US05/03369	International filing date (day/month/year) 04 February 2005 (04.02.2005)	Priority date (day/month/year) 04 February 2004 (04.02.2004)
International Patent Classification (IPC) or both national classification and IPC IPC(7): C12Q 1/02, 1/04 and US Cl.: 435/29, 34		
Applicant JOHNS HOPKINS UNIVERSITY		

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input checked="" type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Dr. Kailash C. Srivastava Telephone No. (703)-308-0196
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Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE
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International application No.

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

10/587927
IAP11 Rec'd PCT/PTO 01 AUG 2006

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Box No. II Priority

1. ☐ The following document has not yet been furnished:

☐ copy of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority has been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

This International Examining Authority acknowledges applicant's claim for priority to Provisional U.S. Application Serial Number 60/541,781 filed 04 February 2004.

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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-49</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>1-38, 46, 48</u>	YES
	Claims <u>39-45 and 48-49</u>	NO
Industrial applicability (IA)	Claims <u>1-49</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Please See Continuation Sheet

**WRITTEN OPINION OF THE
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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 1-38 meet the criteria set out in PCT Articles 33 (2)-(4), because the cited prior art references do not specifically teach a System comprising a sampling device, and all other features for said sampling device instantly claimed to collect and characterize cells from an environmental capillary microcosm via providing a plurality of samples to a characterizing device. Said prior art references also do not teach following independently claimed methods according to each and every step as claimed in the instant invention to:

- (i). characterize cells in a microcosm environment ,
- (ii). optimize a medical treatment for a patient,
- (iii). screen a medical treatment for a patient,
- (iv). diagnose an infectious or a parasitic disease, and
- (v). test effect of an agent on a living organism.

The cited prior art references, only teach the subject matter of the claimed invention in general terms.

Thus, the cited references do not teach or reasonably suggest a device or one of the above-cited methods as claimed. Therefore, the Claimed device or methods are neither anticipated nor lack an inventive step over the cited prior art and therefore, have industrial applicability because the subject matter claimed can be made or used in industry.

Claims 39-49 meet the criteria set out in PCT Article 33(2), because the prior art does not teach the method invention claimed in those claims.

Claims 39-45 and 48-49 lack an inventive step under PCT Article 33(3) as being obvious over Short (U.S. Patent 5,830,696) in view of Isola et al. (Analytical Chemistry, 2001, Volume 73, Pages 2126-2131). Short teaches detecting a thermophilic microorganism producing a thermostable enzyme, wherein said thermophilic microorganism is isolated from an environmental sample obtained from a natural source. Said enzyme has an industrial or biomedical applicability. Production, i.e., activity of said enzyme and yield is enhanced via isolating said enzyme gene and introducing said gene in to a host to produce said enzyme, wherein said host grows at a temperature lower than the growth temperature of said thermophilic microorganism. Said enzyme is a dioxxygenase and the cloning and detection for said enzyme is performed with a cell digest of the thermophilic microorganism originally harboring the thermostable enzyme gene (Column 1, Lines 9-13; Lines 25-33; Column 2, Lines 22-43; Column 4, Lines 21-32; Column 7, Line 12; Column 8, Lines 1-4 and Column 8, Line 35 to Column 10, Line 27). Short has demonstrated the production of said thermophilic enzyme in another host for a beta glycosidase, nevertheless, short teaches that any of the enzymes listed in Columns 6, Line 28-Column 7, Line 62 are the representative enzymes and therefore Short

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

intrinsically teaches that the techniques applicable to one of those enzymes are applicable to other listed enzymes via equivalence. Thus, Short teaches a method to detect a microorganism in an environmental microcosm sample via identifying a phenotype that is a biomarker, wherein said biomarker phenotype is a dioxygenase enzyme that is overproduced in a cell growing at a temperature lower than the growth temperature of the original microorganism from where the enzyme, i.e., phenotype was isolated. Furthermore, Short teaches that said enzyme has an industrial utility. Thus, intrinsically said enzyme production is induced in the producing microorganism and has applicability in bioremediation. Short, however, does not teach identifying said enzyme via mass spectroscopy-peptide fingerprinting. Isola et al teach aMALDI-TOF spectrometric method for peptide finger printing (Page 2126, Column 2, Lines 17-25).

Thus, at the time, the claimed invention was made, an artisan of ordinary skill would have been motivated to combine the teachings from Short with the beneficial teachings from Isola et al., because Isola et al. remedy the deficiency in teachings from Short of a MALDI-TOF spectrometry to fingerprint a peptide, i.e. an enzyme. The prior art methods cited herein do not have the same actual concentrations of all the components as those presently claimed. However, the adjustment of particular conventional working components/conditions (e.g., concentrations of different components of a composition, equivalent components having same properties or same function) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter, which is well within the purview of the skilled artisan. In view of the fact that the applicant's invention also recites a method comprising the same steps and composition and a test strip comprised of same components; applicant's invention is obvious over the teachings of Examiner-cited prior art references and therefore, does not have an inventive step.

Claims 1-32 meet the criteria set out in PCT Article 33(4), and thus Claims 1-32 have industrial applicability because the subject matter claimed can be made or used in industry.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.